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There are a number of possible mechanisms by which the lung can become more vulnerable to microoorganisms. These include (1) reduction in deposition or retention of bacteria, (2) slowing of physical removal of bacterial cells by the mucociliary mechanisms, (3) dysfunction of the alveolar macrophages, (4) alteration of the acellular lining material (surfactant) of the deep lung, (5) the presence of edema fluid or imflammatory exudate in the airway, and (6) pulmonary immunosuppresion. The influence of environmental pollutants on each of these factors is discussed.

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Increased Pulmonary Disease Mediated Through Altered Bacterial Defenses

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ABSTRACT

The process of infection has been defined as an interaction of a host, a microbe, and the environment. In the natural environment, healthy individuals exist in equilibrium with potentially pathogenic microorganisms. Using this concept, an animal-model system was developed to study the effects of pollutants that can affect this equilibrium and result in acute pulmonary disease. Increase of mortality from exposure to several pathogenic organisms has been reported for a variety of animal species after exposure to ozone, nitrogen dioxide, and a variety of trace metals.

There are a number of possible mechanisms by which the lung can become more vulnerable to microorganisms. These include (1) reduction in deposition or retention of bacteria, (2) slowing of physical removal of bacterial cells by the mucociliary mechanism, (3) dysfunction of the alveolar macrophages, (4) alteration of the acellular lining material (surfactant) of the deep lung, (5) the presence of edema fluid or inflammatory exudate in the airway, and (6) pulmonary immunosuppression. The influence of environmental pollutants on each of these factors is discussed.

For many years it has been apparent that most infectious disease states are not the result of a simple one-to-one cause and effect relationship but instead are a reflection of several different influences acting on the host simultaneously. Establishing an infectious disease requires not only a specific microorganism but additional factors that would render a particular individual vulnerable to microbial invasion. Various factors that weaken host resistance, such as stress,[1-4] preexisting disease,[5] dietary deficiencies,[6] etc., can modify the pathogenesis of the infection. Thus disease is a product of multiple

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factors, and the interaction of these factors with the prime etiologic agent has been described as the principle of multiple causality.

Traditionally, environmental toxicologists have been primarily concerned with measuring and describing effects of such single toxic agents[7-11] as O_3, SO_2, and NO_2. More recently, studies have begun to examine the role of multiple pollutants as a modifier of host resistance to experimental infection.

Owing to the inherent problems associated with the study of the effects of pollutants on the susceptibility of the human respiratory system to microbial infection, animal-model systems have been developed to investigate various hypotheses that can later, through appropriate epidemiological surveys, be tested on man. The animal model for this microbe—host interaction system must be a sensitive one for measuring the subtle effects resulting from inhalation of toxic substances. The model should therefore reflect a summation of the varied responses of the respiratory tract, which may include edema, cellular disruption, reduced macrophage function, inflammation, and immunosuppression. The influence of atmospheric pollutants on the microbe—host interaction is difficult to predict because the test substance may increase, decrease, or have no effect on the susceptibility of the host to infection. Also, the host response is dependent on several conditions: (1) the concentration of the pollutant, (2) the physiological state of the host and of the microbial development on and in the host, and (3) the length of time between pollutant exposure and microbial exposure.

A number of different experimental approaches have been used to demonstrate the potential of chemical agents for altering host susceptibility to respiratory infectious agents. One of the most sensitive methods is used by a number of laboratories, including ours, and is called the infectivity model (Fig. 1). Briefly, animals are randomly selected for exposure either to filtered room air or to the test substance. After the cessation of this exposure, the animals from both chambers are combined into a third chamber where they are exposed for approximately 15 min to an aerosol of viable microorganisms. In our laboratory, we routinely use *Streptococcus pyogenes*, Group C. At the termination of this exposure, some animals from each group are sacrificed, and, using standard microbiological techniques, the number of inhaled microorganisms at 0 hr is determined. The remainder of the animals are returned to clean filtered room air, and the rate of mortality in the two groups is determined during a 15-day holding period. The control mortality, which reflects the natural resistance of the host to the infectious agent, is approximately 15 to 20%. This system can also be expanded

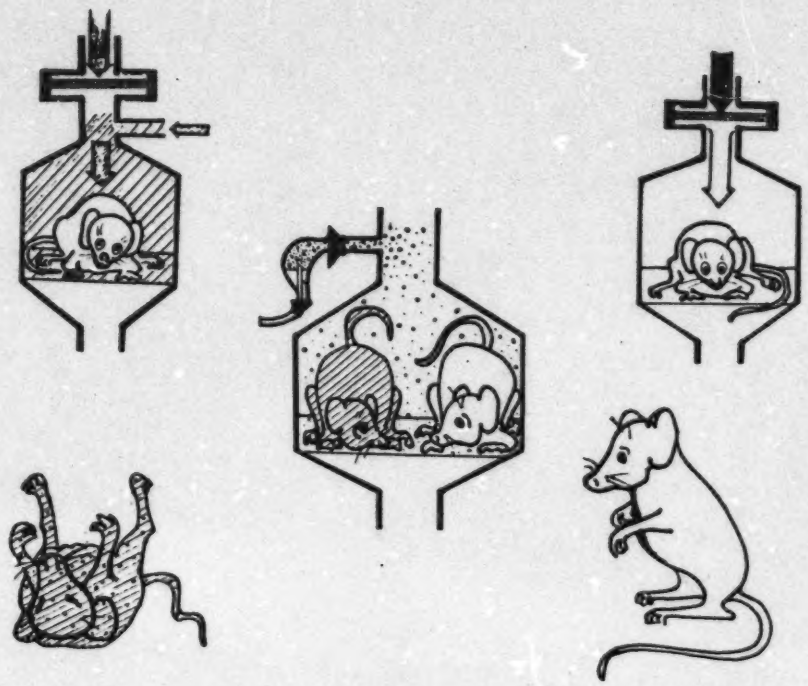

Fig. 1 Infectivity model. Upper left, mouse exposed to pollutant. Upper right, mouse exposed to clean air. Center, pollutant-exposed and air-treated mice challenged with aerosols of bacteria. Lower left, mortality of pollutant-exposed mouse. Lower right, survival of air-exposed mouse.

to permit observation of altered pathogenic modes, relative mean survival time, and cytological indices of isolated lung cells.

For an effective infectivity-model system, the microorganism must fulfill certain criteria. The infectivity model must cause a rather low mortality rate in animals not exposed to the toxicant, and the mortality rate must not be greatly influenced by small variations of bacterial doses or virulence from test to test. Methods must be available for consistently administering the organisms in an aerosol at a concentration and size necessary for pulmonary deposition and for measuring the bacterial dose.

This infectivity-model system, using a number of different microorganisms (*Diplococcus*, *Klebsiella*, *Streptococcus*, influenza virus), has been successfully used with a variety of animal species,

including the mouse,[7-11] rat,[12] hamster[13] and squirrel monkey.[14] Inhalation of a number of noxious gases has been shown to increase mortality in this system.[7-11] As shown in Fig. 2, NO_2 exposure strikingly enhances mortality in mice exposed to streptococci. This family of curves illustrates how the enhancement in mortality can be related to the duration of a continuous exposure at different concentrations of NO_2. Similar studies were performed by Ehrlich,[15] who exposed three species of laboratory animals to NO_2 with a subsequent challenge with *Klebsiella pneumoniae*. Nitrogen dioxide was toxic for all species, and the results also indicate the resistance of each species to the gas and bacteria. Mice were the most sensitive, as evidenced by the data, which showed significant excess mortality at $\geq$ 6.58 mg/m^3 (3.5 ppm). Squirrel monkeys were the least sensitive, with 94.05 mg/m^3 (50 ppm) required for significant effect. Hamsters, which exhibited enhanced mortality at $>$ 65.83 mg/m^3 (3.5 ppm), had intermediate sensitivity.

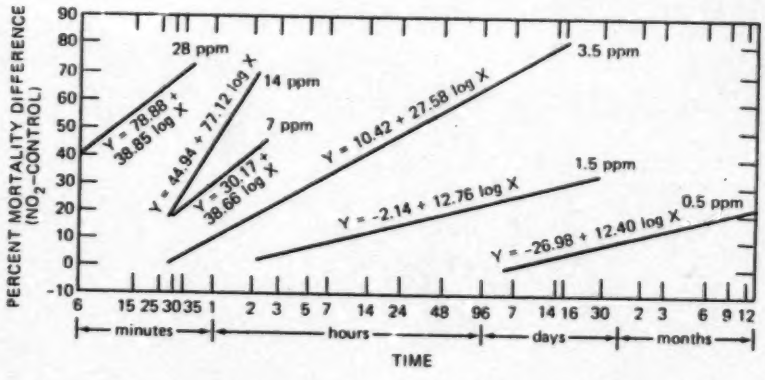

Fig. 2 Percent mortality of mice versus length of continuous exposure to various NO_2 concentrations prior to challenge with streptococci.

Using the infectivity model,[7] experimenters found that exposure of mice to an O_3 concentration between 196 and 392 μg/m^3 (0.1 and 0.2 ppm) and higher for 3 hr also elicits enhancement of mortality (Fig. 3). Various environmental stresses have been shown to further enhance the O_3 effect. Exposure to either reduced or elevated temperatures after a bacterial aerosol challenge results in greater mortality than was produced by either treatment alone.[16]

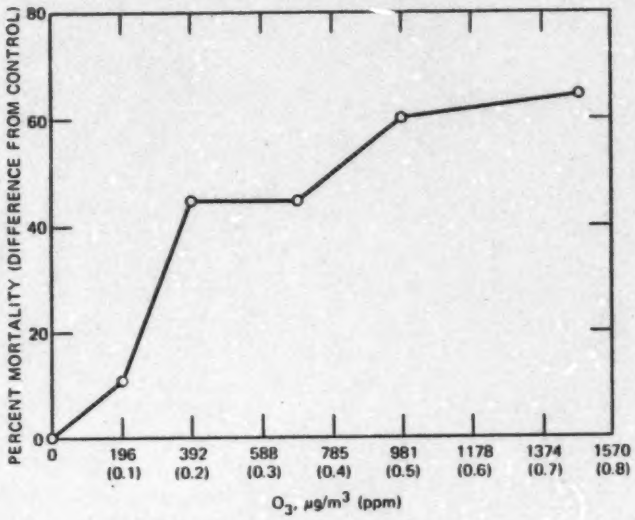

Fig. 3 Effect of a 3-hr exposure to various concentrations of O_3 on mice challenged with aerosols of *Streptococcus*.

Exercise during the exposure of the test animals to either O_3 or NO_2 also appears to enhance the toxicity of the pollutant, as evidenced by increased mortality rates due to infection.[4] Figure 4 illustrates the effect of exercise on mice exposed to NO_2.

Exposure to aerosols of such trace metals[17-19] as $NiCl_2$, PtO_2, and $CdCl_2$ also has a marked proclivity to reduce the ability of the lung to defend itself against microbial insults. As Fig. 5 indicates, an increase of approximately 20% ($p < 0.05$) in percent mortality above controls was observed following a 2-hr exposure to 100 μg Cd/m^3, whereas, with $NiCl_2$, a concentration of 500 μg Ni/m^3 was necessary to obtain a significant increase in mortality. Even though $NiCl_2$ also enhanced the mortality rate, the mechanism of toxicity appears to be somewhat different. When animals that were challenged with viable streptococci immediately were compared to those exposed to the bacteria 24 hr following the nickel treatment, a significantly greater enhancement of mortality was observed in the 24-hr group. No such delay in time effect was observed in the experiment using cadmium.

If host defense mechanisms are functioning normally, there is rapid inactivation of inhaled bacteria that have penetrated and been deposited at the alveolar level.[20-26] However, quite the opposite occurs in pollutant-exposed animals. The number of microbes in the

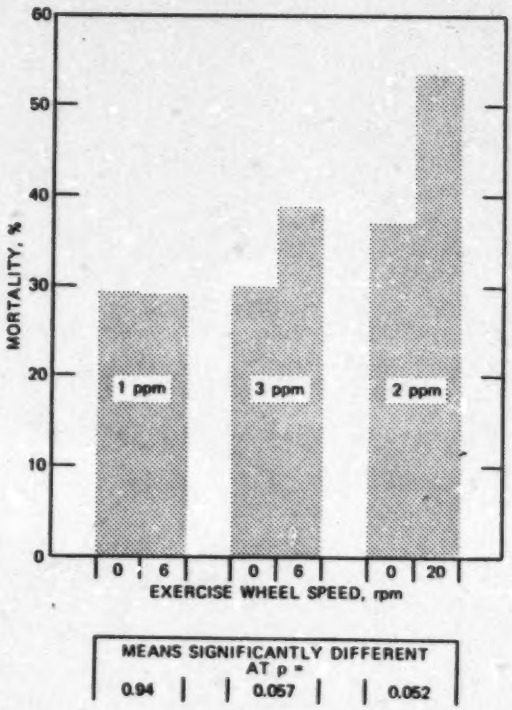

Fig. 4 Influence of exercise on NO_2 toxicity using the infectivity-model system. Mice were exposed to various concentrations of NO_2 for 3 hr, with and without exercise (running on a wheel at the indicated rpm) prior to an aerosol of *Streptococcus*.

lungs of exposed mice quickly multiply and soon increase beyond the original number deposited[7,17,19] (Fig. 6). This acceleration in the rate of bacterial growth has been attributed to the pollutant's alteration of the capability of the lungs to destroy bacteria so as to permit those with pathogenic potential to multiply and produce disease. Such a concept is supported by the work of Goldstein et al.,[21-23] who exposed mice to O_3 and NO_2 alone and together and to aerosols of radiolabeled staphylococci. Their results indicate that these pollutants are capable of reducing the bactericidal activity of the lung. Higher O_3 levels actually resulted in a net multiplication of bacteria. Thus the role of environmental agents in the pathogenesis of infectious pulmonary disease may be mediated through an

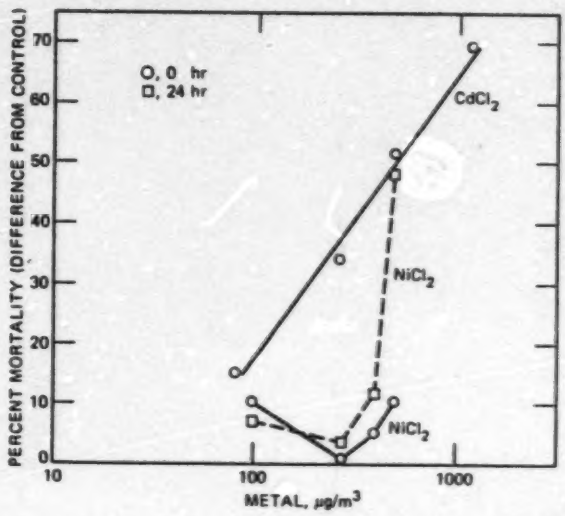

Fig. 5 Toxicity of a 2-hr aerosol exposure to various concentrations of $CdCl_2$ and $NiCl_2$ using the infectivity-model system. ○, mice challenged with an aerosol of *Streptococcus* immediately following metal exposure. □, mice challenged with an aerosol of *Streptococcus* 24 hr following metal exposure.

impairment of integrated pulmonary-host defense functions that maintain sterility in the deep lung.

A number of possible mechanisms can be proposed which might aid in explaining how gaseous and particulate pollutants reduce the ability of the lung to defend itself against the growth of these inhaled microbes. These mechanisms include (1) production of edema, (2) reduction in physical removal by mucociliary mechanisms, and/or (3) alteration of specific cellular defense mechanisms. Each of these possible mechanisms has been studied, and the data obtained provide information that aids in explaining the enhancement of infectivity phenomena.

First, if the test substance caused an influx of edema fluid into the lung, this would provide an ideal culture medium for microbial growth. Tests were designed to determine if edema might play a major role in the enhancement of pulmonary infection. These experiments used O_3, which has been shown to be edemagenic and which also causes enhancement of infections. This study was based on findings of numerous investigators who have reported that, by

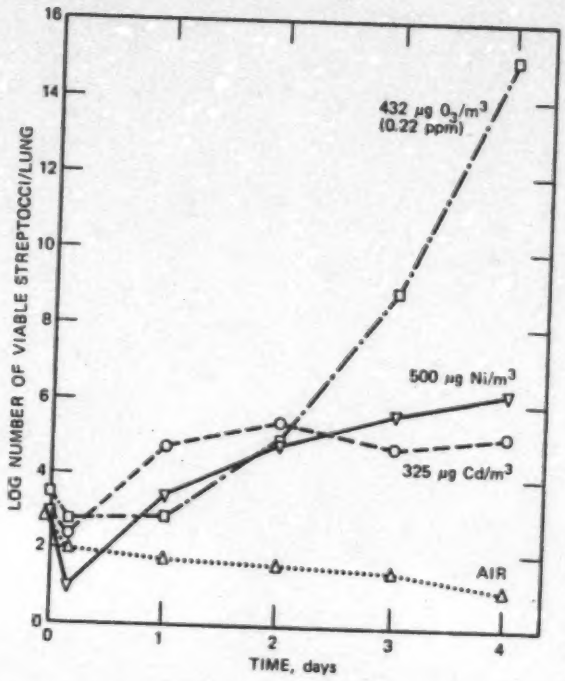

Fig. 6 Growth of streptococci in the lungs of mice exposed to O_3 for 3 hr, metal aerosols for 2 hr, or air for 2 hr prior to challenge with aerosols of bacteria.

repeating O_3 exposures, a protective state (tolerance) against the subsequent production of edema[3,27,28] can be produced. In these classical studies, preexposure to a tolerant dose of O_3 protects the animal from death due to exposure to an acute toxic concentration of O_3 by significantly reducing edemagenesis.[29,30] When experiments were conducted to detect changes in infectivity with a system designed to elicit tolerance, the tolerant animals showed only partial reductions in mortality, compared to animals receiving a single O_3 exposure. Figure 7 illustrates that the mortality is reduced only about one-half in animals preexposed to a tolerant dose of O_3 at a concentration of 588 $\mu g/m^3$ (0.3 ppm) or higher. At 196 $\mu g/m^3$ (0.1 ppm), there is no significant difference imparted by the preparatory or tolerance-eliciting exposure. These results differ significantly from the classical criteria of edema formation used in tolerance studies.

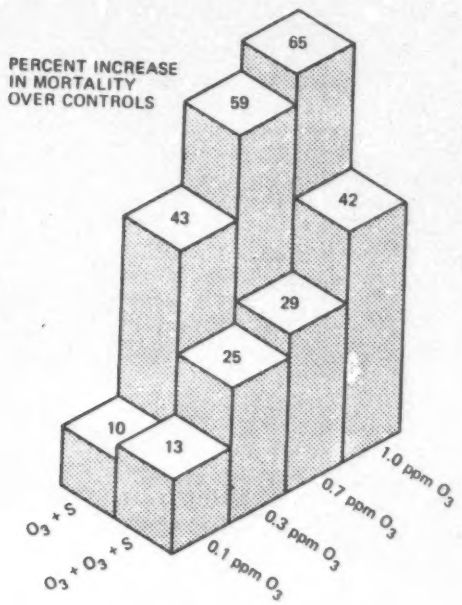

Fig. 7 Influence of a tolerance-inducing dose of O_3 on the infectivity-model system at various O_3 concentrations. O_3 + S, 3 hr of O_3 prior to streptococcal challenge. O_3 + O_3 + S, 3 hr of O_3, 24 hr of clean air, and 3 hr of O_3 prior to streptococcal challenge.

If tolerance were as effective in preventing pulmonary infection as it is in preventing edema, a complete protection against mortality should be evident. That is, the percent increase in mortality over non-O_3-exposed controls should be essentially zero. The data suggest that, since there is partial protection, O_3 may be affecting specific body defenses (possibly alveolar macrophages) which are not protected by the phenomenon of tolerance. This is in agreement with earlier studies by Gardner et al.[31] which showed that preexposure to O_3 produced a tolerance against pulmonary edema but had no protective effect against the cytotoxic effects of O_3 on alveolar macrophages, such as reduction in numbers, viability, and hydrolytic enzyme activities. Another reason why edema does not appear to be solely responsible for the microbial growth in the lung is that enhancement of respiratory infections has been shown at levels[7] lower than those which produce edema in experimental animals.[32]

A second mechanism by which environmental contaminants may impair host defenses possibly occurs through the alteration of the mucociliary escalator, which could lead to increased bacterial burdens in the lung. Adalis et al.[33,34] studied the beating frequency of cilia isolated from the trachea of hamsters that were exposed to aerosols of $CdCl_2$ or $NiCl_2$. Although these metals reduced the ciliary activity, the metal concentrations that produced these effects were lower than the concentrations that enhance mortality in the infectivity model. Thus the slowing of ciliary beating does not appear to be the sole cause of the increased bacterial growth observed in the infectivity system. The lack of relationship between defects in the mucociliary escalator and increased bacterial growth is also evident from studies by other investigators, such as Rylander,[35] Kim et al.,[24] Kass, Green, and Goldstein,[20] Goldstein, Lippert, and Warshauer,[26] and Green and Goldstein.[25] Green and Kass,[36] using radiolabeled microorganisms, found that physical removal could account for only a small fraction (15 to 20%) of the total bacteria cleared from the lung over a 4-hr period. These studies clearly demonstrate that the loss of viable microorganisms results primarily from in situ bactericidal activity rather than from mechanical removal.

After we discount the defects in the physical removal and the edema production as the only causes of enhanced bacterial growth in the lungs of pollutant-exposed animals, just one major protective mechanism remains—that of biological clearance. This type of clearance primarily reflects the role of the alveolar macrophage. An interesting in-vivo model described by Green and Goldstein[25] and Kim et al.[24] supports this classical contention. In this system, mice were exposed to aerosols of *Staphylococcus aureus*, and the intra- or extracellular locations of bacteria were determined histologically in the right lung, and the number of viable organisms were determined bacteriologically in the left lung. These investigators showed that phagocytosis of the staphylococci by alveolar macrophages precedes and roughly parallels the actual clearance of the bacteria for a time period of less than 2.5 hr. After this time, phagocytosis reaches a plateau, whereas bactericidal activity continues to increase. Since the alveolar macrophage is therefore primarily responsible for biological clearance, bacterial growth in the lungs due to pollutant exposure is probably a reflection of decreased pulmonary bactericidal ability, which, in turn, is caused by dysfunction of alveolar macrophages.

Pollutant-exposed alveolar macrophages have been the subject of intensive investigation. Aranyi et al.[37] and Waters et al.[38] used scanning electron-microscopy techniques to demonstrate direct

surface alteration of alveolar macrophages caused by exposure to O_3, NO_2, O_2 and a number of trace metals.

Figure 8 illustrates membrane alterations of alveolar macrophages exposed to O_3 and NO_2. The authors conclude that such morphological data may be useful in detecting changes that precede cell death. Experiments conducted in our laboratory have indicated that in vivo exposure to such pollutants as O_3 (Refs. 7 and 39), NO_2 (Ref. 40), and $CdCl_2$ (Ref. 19) have the potential to produce decrements in number, viability, phagocytic activity, and enzymatic activity in macrophages obtained by pulmonary lavage. Bingham et al.[41,42] measured the total number of available alveolar macrophages lavaged from rats exposed to $PbCl_2$, $NiCl_2$, Pb_2O_3, and NiO. The NiO produced a significant increase in the number of free cells, and the Pb_2O_3 resulted in fewer cells. The other two substances did not significantly change the number of available cells.

In vitro studies performed on alveolar macrophages have substantiated many of the above cytotoxic effects with O_3 (Ref. 43), cigarette smoke (Ref. 44), V_2O_5 (Refs. 38, 45, and 46), $MnCl_2$ (Refs. 38 and 45), $NiCl_2$ (Refs. 38 and 45), $CdCl_2$ (Refs. 38 and 45), $CrCl_3$ (Refs. 38 and 45), NO_2 (Refs. 47 and 48), and ethanol (Ref. 49).

In addition to the direct action of the pollutant on the alveolar macrophages, it is also possible that some pollutant toxicity to the alveolar macrophages could be mediated through an indirect effect. Gil and Weibel[50] demonstrated that, within the lung, the alveolar macrophages and the acellular lining substance are intimately associated. Alveolar macrophages appear to be immersed in this substance. Figure 9 is a dose-response curve that illustrates the effect of the in vivo action of O_3 on the stability of alveolar macrophages in vitro.[51] When normal alveolar macrophages are resuspended in normal acellular lavage fluid, the number of cells remain relatively stable (15% lysis) over a 4.5-hr test period. However, if these same normal cells are placed in lavage fluid from animals exposed to O_3 for 3 hr, an increase in cell lysis occurs over the 4.5-hr test period. If both the macrophages and the lavage fluid are from animals exposed to O_3, then stability is severely affected. Figure 10 illustrates that similar effects can be produced when normal lavage fluid is exposed in vitro to O_3 for 30 min. For these in vitro experiments to be valid, the measured response must be due to the action of O_3 on the fluid itself and not due merely to the physical action of bubbling. Table 1 shows the percent of alveolar macrophages remaining after various times when other gases (room air, nitrogen, carbon dioxide) were bubbled through the lavage fluid for a 30-min period. There was no statistically significant difference between normal lavage fluid and

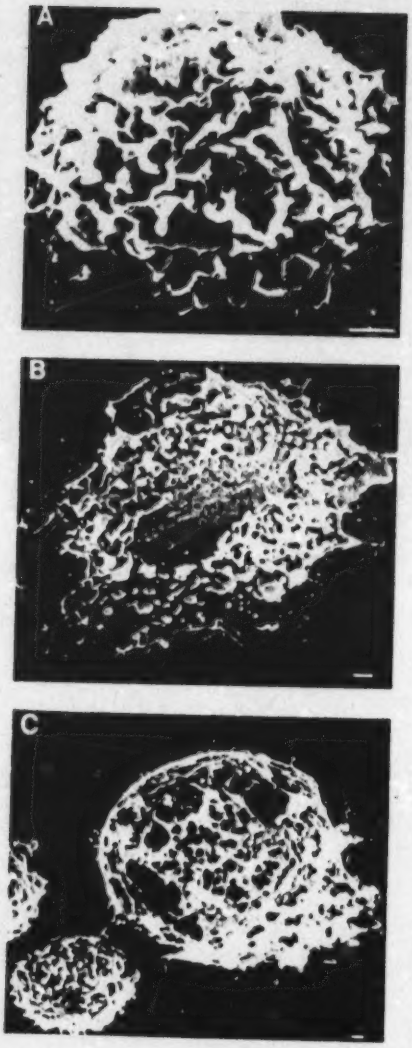

Fig. 8 Scanning electron-microscopic view of alveolar macrophages. Bars represent 1 μm. (A) Alveolar macrophages from a mouse exposed to filtered air. (B) Alveolar macrophages from a mouse exposed to 940.5 $\mu g/m^3$ (0.5 ppm NO_2) continuously for 21 wk with 1-hr peaks of 3762 $\mu g/m^3$ (2 ppm NO_2) five times a week. (C) Alveolar macrophages from a rabbit exposed to 5780 $\mu g/m^3$ (3 ppm O_3) for 3 hr.

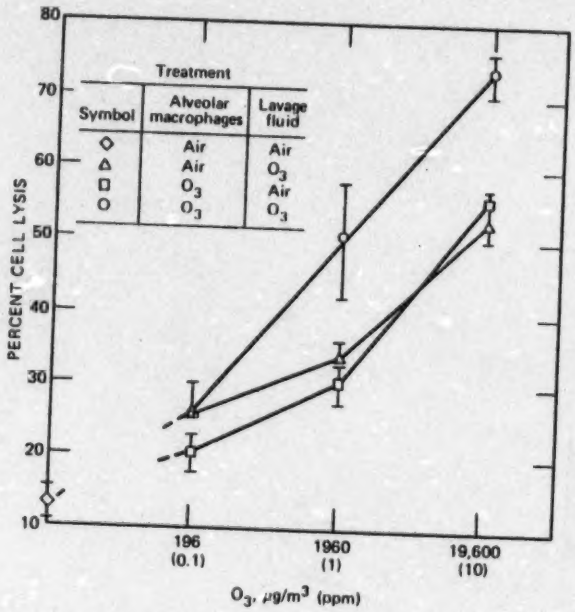

Fig. 9 Influence of various concentrations of O_3 on the percent cell lysis of alveolar macrophages from air- and O_3-exposed rabbits maintained in pulmonary lavage fluids from both air- and O_3-exposed rabbits. Animals were exposed for 3 hr. Points on the graph are mean level ± standard error.

lavage fluid exposed to nitrogen or carbon dioxide. The exposure to filtered room air appeared to affect the stability of the alveolar macrophage, but not to the same extent as O_3. Thus the increase in cell lysis appears to be due to the direct action of O_3 on the protective factor, which, in turn, results in secondary lysis of the alveolar macrophages.

Studies were also conducted to determine what effect the lavage fluid might have on the ability of the alveolar macrophage to phagocytize yeast cells (*Saccharomyces cerevisiae*)[51] (Table 2). Normal macrophages that were suspended in saline phagocytized the least (31%), but, as was expected, the phagocytosis was improved by the addition of 20% rabbit serum to the physiological saline. There was no significant difference in the phagocytic ability of alveolar macrophages in normal lavage fluid, as compared to in vitro O_3-treated (19,600 μg/m³, 10 ppm) lavage fluid. The alveolar

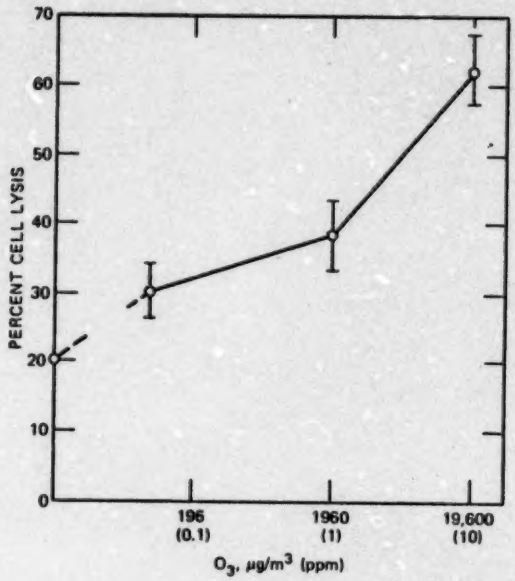

Fig. 10 Percent cell lysis of alveolar macrophages from air-exposed rabbits maintained in pulmonary lavage fluid treated with the indicated concentrations of O_3 for 30 min.

TABLE 1

INTEGRITY OF ALVEOLAR MACROPHAGES FROM NORMAL RABBITS MAINTAINED IN NORMAL LAVAGE FLUID TREATED WITH DIFFERENT GASES FOR 30 min

(Values Are Expressed as Mean ± Standard Error)

Suspended in	Percent of cells remaining at 4.5 hr
L.F.*	81.0 ± 1.2
L.F. + N_2	76.6 ± 3.6
L.F. + CO_2	76.6 ± 1.7
L.F. + room air	68.5 ± 4.0
L.F. + O_3	35.0 ± 4.0

*L.F. = lavage fluid.

TABLE 2

PHAGOCYTIC CAPABILITY OF NORMAL ALVEOLAR MACROPHAGES MAINTAINED IN VARIOUS LAVAGE FLUIDS

(Values Are Expressed as Mean Level ± S.E.*)

Normal cells suspended in	10^6 alveolar macrophages per milliliter ($\bar{X}$† ± S.E.)		Percent of alveolar macrophages remaining at 1 hr ($\bar{X}$ ± S.E.)	Alveolar macrophages/yeast ratio ($\bar{X}$ ± S.E.)		Percent of alveolar macrophages with yeast ($\bar{X}$ ± S.E.)
	0 hr	1 hr		0 hr	1 hr	
Normal L.F.‡	3.63 ± 0.30	3.23 ± 0.31	88.5 ± 1.7	1:26 ± 3	1:29 ± 3	43.8 ± 3.4
Ozone L.F. in vivo	3.54 ± 0.26	2.71 ± 0.27	76.1 ± 2.8	1:26 ± 3	1:35 ± 4	80.8 ± 3.8
Ozone L.F. in vitro	2.92 ± 0.45	2.90 ± 0.29	72.2 ± 1.9	1:34 ± 6	1:47 ± 8	46.2 ± 8.1
Saline	2.55 ± 0.38	1.69 ± 0.31	66.8 ± 6.8	1:41 ± 10	1:66 ± 14	30.8 ± 3.6
Saline + 20% rabbit serum	2.42 ± 0.11	2.2 ± 0.11	90.9 ± 0.4	1:40 ± 2	1:44 ± 2	58.5 ± 3.9

*S.E. = standard error.
†$\bar{X}$ = mean level.
‡L.F. = lavage fluid.

macrophages exhibiting the greatest phagocytic activity (81%) were those normal macrophages which were maintained in lavage fluid harvested from rabbits exposed to 19,600 $\mu g/m^3$ (10 ppm) of O_3 for 2.5 hr. This twofold increase in phagocytosis, as compared to those suspended in normal or in vitro-treated lavage fluid, was thought to be due to an increased protein content of the edema fluid, a typical pulmonary response to this high level of O_3. As this experiment showed, the addition of serum to physiological saline increased the phagocytic ability from 31 to 58%. It was interesting to observe that exposure to O_3 did not adversely affect the phagocytic functioning of normal alveolar macrophages in vitro, but it must be pointed out that, in obtaining the phagocytic index, only remaining intact macrophages were counted. As Table 2 shows, the alveolar macrophages that were held either in O_3-treated lavage fluid or in saline had fewer cells remaining, as compared to those alveolar macrophages which were held in normal lavage fluid.

Other studies have been conducted with this pulmonary protective factor. The data of LaForce, Keely, and Huber[52] suggest that this protective factor can also stimulate the bactericidal activity of alveolar macrophages against *Staphylococcus aureus*. Without the isolated alveolar lining material, no bactericidal effect could be shown. From these studies it becomes important for toxicologists to consider the interaction of environmental pollutants with the intrapulmonary milieu, as well as the cells in the lung, before assuming that the pollutant has a direct action on the alveolar macrophages.

Most of the foregoing discussion has centered on the "classical" role of alveolar macrophage phagocytosis and bacterial lysis, but the possible role of pollutant-induced immunosuppression cannot be ignored; the possible importance of the immune system to pulmonary defense must be considered. Although the actual role of the alveolar macrophages in the pulmonary immune system is still a matter of debate, several investigations provide data on this topic. Seeger and Oppenheim,[53] and Ulrich[54] have demonstrated that alveolar macrophages can enhance immune responses of lymphocytes. Other work by Martin and Laughter[55] showed that alveolar macrophages from cigarette smokers were less able to stimulate lymphocyte activity. Most of the knowledge in the area of pollutant effect on the respiratory immune system is derived from the work of Zarkower,[56] who exposed mice to various air pollutants prior to an aerosol immunization with *Escherichia coli*. Long-term exposure to SO_2 and carbon and to carbon + SO_2 reduced serum antibody titers, and, in addition, the treatment of carbon + SO_2 caused a reduction

in antibody-producing cells in the mediastinal lymph nodes that drain the lung. Miller and Zarkower[5 7] also reported that aerosols of SiO_2 were capable of reducing the functioning of lymphocytes and the number of antibody-forming cells in the mediastinal lymph nodes, and, again, serum antibody titers were reduced. Since this silica-dust treatment also depressed phagocytosis by alveolar macrophages, it is possible that some of these immunosuppressive effects were mediated through the cytotoxic effects of SiO_2 on alveolar macrophages.

Perhaps the difficulty in determining the actual mechanism responsible for the pollutant-induced increase of bacterial growth in the lung and subsequent mortality observed in the infectivity-model system is because there are many possible causes for this phenomenon. It is probable that the large number of pathophysiological changes that occur following pollutant exposure can alter an individual's homeostatic balance, yielding a reduced capacity to recuperate from pulmonary infectious challenges.

As is obvious from this discussion, much more information is needed to determine the total range of the functions of alveolar macrophages and the impact of pollutants on these essential cells.

The papers presented at this symposium and in this session will elucidate some of these problem areas. Many of the papers describe investigations of the mechanisms involved in several macrophage functions. The secretory role of alveolar macrophages was studied from the standpoint of release of any possible chemotactic factors and lysosomal enzymes. This latter research has a bearing on another paper in these proceedings which describes the extracellular lysis of bacteria by secreted lysozyme. One work dealing with the renewal of alveolar macrophage populations is also reported.

The results from these research efforts are particularly relevant to the understanding of pollutant effects on the alveolar macrophage, which is the subject of a number of other papers in these proceedings. Phagocytic functioning was investigated following exposure of alveolar macrophages to cigarette smoke and tobacco substitutes and to fly-ash particles coated with metal oxides. Alveolar macrophages from O_3- and NO_2-treated animals were used in studies of membrane receptors, which may be involved in cell recognition and phagocytosis. Other research described involved such parameters as cytostructure, enzymes, tritiated thymidine uptake, and numbers of alveolar macrophages in animals exposed to both clean air and NO_2.

The work reported at this session presents interesting and important information on the functioning of the alveolar macro-

phages and the serious hazards that pollutants present to these important cells. As with all excellent research, we will leave here with more questions than answers, but we still will have advanced ourselves on the continuum of knowledge.

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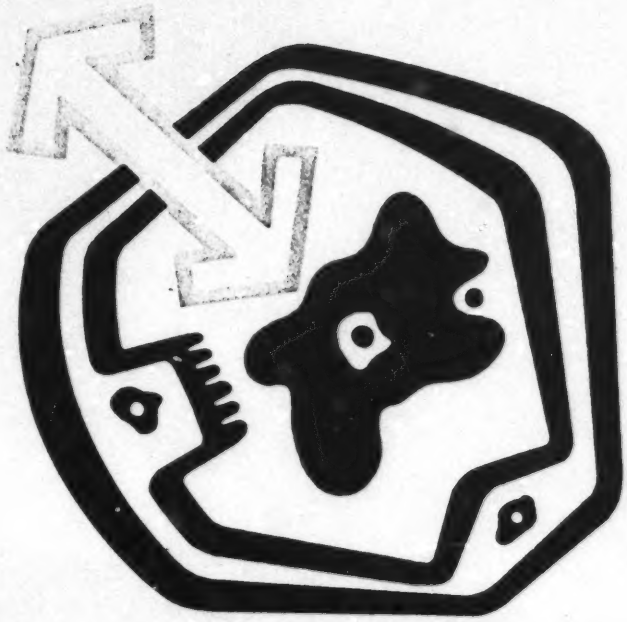

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